Dose-Reduced Pola-R-CHP for Frontline Treatment of Diffuse Large B-Cell Lymphoma in Elderly and Comorbid Patients

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Introduction

The phase III POLARIX trial established polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone (pola-R-CHP) as superior to standard rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) by improving progression-free survival in previously untreated adults with intermediate- to high-risk diffuse large B-cell lymphoma (DLBCL).[1-4] These findings have increased interest in frontline polatuzumab use, though its application in elderly, frail, or comorbid patients remains unclear.[4] Many such patients cannot tolerate full-dose regimens, prompting dose reduction to balance efficacy and toxicity.[5] Dose–attenuated R-CHOP (R-mini-CHOP) has long been the standard for this population, but data on a reduced-intensity pola-R-CHP regimen (pola-R-mini-CHP) are scarce.[5-7] We therefore conducted a retrospective analysis to assess its safety, tolerability, and outcomes in elderly and medically complex patients with DLBCL.

Purpose

The purpose of this study is to evaluate the safety, tolerability, and preliminary efficacy of pola-R-mini-CHP as frontline therapy for elderly, comorbid patients with newly diagnosed DLBCL. In this population, balancing disease control with treatment-related toxicity is a central challenge, and current standard therapies such as R-mini-CHOP offer only modest outcomes.[5-7] By assessing response rates, survival, and adverse event profiles, we aim to determine whether pola-R-mini-CHP can provide an acceptable therapeutic balance and serve as a potential alternative to existing reduced-intensity regimens.

Methods

We retrospectively analyzed 17 patients aged ≥70 years with newly diagnosed DLBCL and Charlson Comorbidity Index (CCI) ≥2 who received pola-R-mini-CHP at NYU Langone Health between August 2022 and December 2024 (data cutoff: May 5, 2025). Treatment consisted of cyclophosphamide (375–600 mg/m²) and doxorubicin (25–40 mg/m²) with standard dosing of polatuzumab vedotin, rituximab, and prednisone every 21 days for six cycles. Outcomes included PFS, CRR, ORR, and OS; safety assessments captured grade 3–4 adverse events, treatment-related deaths, and relative dose intensity (RDI) of cyclophosphamide and doxorubicin relative to full-dose Pola-R-CHP.

Results

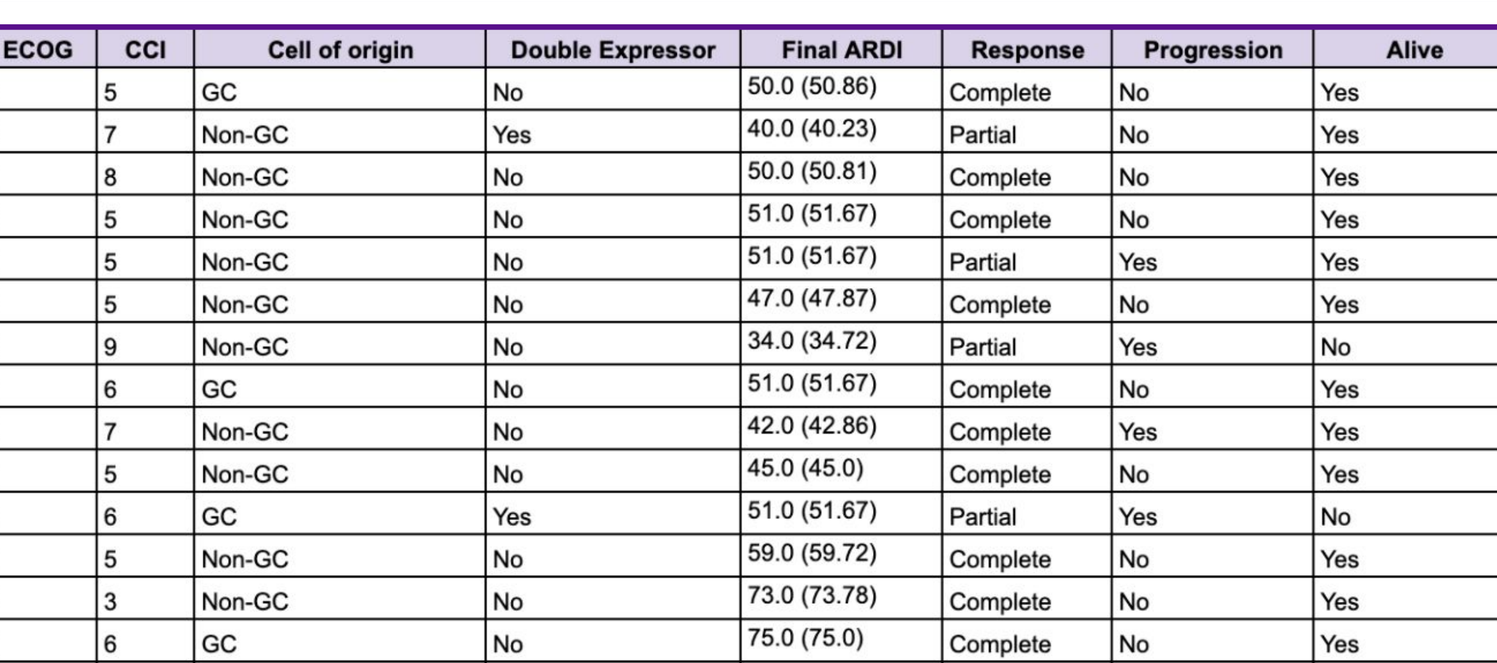
The cohort (median age 74, 59% male) was characterized by frequent high-risk features, including non-GCB subtype in 65% (11/17), Lugano stage ≥3 in 82% (14/17), IPI ≥2 in 100%, ECOG ≥2 in 35% (6/17), and a median CCI of 6. With a median follow-up of 10.5 months (range 3.8–22.5), the cohort had a median RDI of 51% (34–80%). Pola-R-mini-CHP achieved an ORR of 100% (17/17) and a CRR of 76% (13/17). Median PFS and OS were not reached; estimated PFS was 88% at 6 months (15/17) and 71% at 12 months (12/17), and estimated 12-month OS was 88% (15/17). CRR trended with RDI: no patients with RDI ≤40% achieved CR, compared with 15/17 (88%) with RDI >40%. A total of 20 grade 3–4 adverse events were observed in 65% of patients (11/17), with two early discontinuations and three deaths (one on-treatment, two overall).

Figures

Age	Sex	Race	BMI	ECOG	CCI	Cell of origin	Double Expressor	Final ARDI	Response	Progression	Alive
89	Male	White	25.53	2	5	GC	No	50.0 (50.86)	Complete	No	Yes
84	Female	Hispanic or Latino or Spanish	17.39	3	7	Non-GC	Yes	40.0 (40.23)	Partial	No	Yes
82	Male	White	22.45	1	8	Non-GC	No	50.0 (50.81)	Complete	No	Yes
80	Female	White	17.68	1	5	Non-GC	No	51.0 (51.67)	Complete	No	Yes
79	Male	White	20.36	1	5	Non-GC	No	51.0 (51.67)	Partial	Yes	Yes
74	Male	White	23.74	2	5	Non-GC	No	47.0 (47.87)	Complete	No	Yes
74	Female	Hispanic or Latino or Spanish	30.87	2	9	Non-GC	No	34.0 (34.72)	Partial	Yes	No
71	Female	Asian	29.54	1	6	GC	No	51.0 (51.67)	Complete	No	Yes
71	Male	Asian	24.6	1	7	Non-GC	No	42.0 (42.86)	Complete	Yes	Yes
72	Female	White	42.17	1	5	Non-GC	No	45.0 (45.0)	Complete	No	Yes
80	Male	White	18.78	4	6	GC	Yes	51.0 (51.67)	Partial	Yes	No
78	Female	White	26.91	1	5	Non-GC	No	59.0 (59.72)	Complete	No	Yes
76	Male	White	31.41	0	3	Non-GC	No	73.0 (73.78)	Complete	No	Yes
74	Male	White	42.77	1	6	GC	No	75.0 (75.0)	Complete	No	Yes
72	Male	American Indian	26.63	0	7	Non-GC	No	80.0 (80.0)	Complete	No	Yes
70	Male	Hispanic or Latino or Spanish	29.16	1	7	GC	No	80.0 (80.64)	Complete	No	Yes
73	Female	White	26.28	3	3	GC	No	51 (51.67)	Complete	No	Yes

Table 1. Baseline characteristics of 17 patients with newly diagnosed DLBCL treated with pola-R-mini-CHP. Median age 74 years; 59% male; 65% non-GC subtype; median CCI 6. Median RDI 51% (range 34–80%), with an ORR of 100% and CRR of 76%.

Figure 1. Kaplan–Meier estimates of progression-free survival (PFS) and overall survival (OS) in 17 patients with newly diagnosed DLBCL treated with pola-R-mini-CHP. With a median follow-up of 10.5 months, median PFS and OS were not reached; estimated PFS was 88% at 6 months and 71% at 12 months, and estimated 12-month OS was 88%.



Discussion

In this retrospective study of elderly and comorbid patients with newly diagnosed DLBCL, pola-R-mini-CHP demonstrated encouraging efficacy and a manageable safety profile. Despite a median RDI of only 51%, the regimen achieved a 100% ORR and a 77% CRR, with promising early PFS and OS estimates. Compared with historical reports of R-mini-CHOP, outcomes with pola-R-mini-CHP appear favorable, though analysis is limited by study design and limited follow-up durations[5-7]. Notably, patients who received >40% RDI had markedly better complete response rates, suggesting a potential dose-response relationship even within a reduced-intensity framework. While grade 3–4 adverse events were common, occurring in nearly two-thirds of patients, treatment-related mortality was limited. These findings support pola-R-mini-CHP as an induction strategy in older, high-risk DLBCL populations who are not candidates for standard full-dose therapy, and they warrant further investigation in larger, prospective cohorts.

Conclusion

Pola-R-mini-CHP appears feasible for elderly, comorbid patients with newly diagnosed DLBCL, achieving high response rates and encouraging early survival with manageable toxicity. Outcomes are comparable to historical reports of R-mini-CHOP when adequate dose intensity is maintained, suggesting a potential role for polatuzumab in dose-reduced regimens. Larger prospective studies with longer follow-up are needed to fully characterize efficacy, safety, and durability of response in this high-risk population.

References

1. Tilly H, Morschhauser F, Sehn LH, et al. *Polatuzumab vedotin in previously untreated diffuse large B-cell lymphoma*. N Engl J Med. 2022;386(4):351-363. doi:10.1056/NEJMoa2115304
2. Song Y, Tilly H, Rai S, et al. Polatuzumab vedotin in previously untreated DLBCL: an Asia subpopulation analysis from the phase 3 POLARIX trial. Blood. 2023;141(16):1971-1981. doi:10.1182/blood.2022017734
3. Li M, Li Q, Zhang Y, Xu C, Chen Z, Huang Y, Jiang L. Cost-effectiveness of polatuzumab vedotin plus chemoimmunotherapy for untreated diffuse large B-cell lymphoma in China. *Sci Rep*. 2025;15(1):29752. doi:10.1038/s41598-025-15477-9
4. Ghione P, Salles G. Spotlight on polatuzumab vedotin: new standards for diffuse large B-cell lymphoma? *Haematologica*. Published online May 30, 2024. doi:10.3324/haematol.2022.282362
5. Hu B, Reagan PM, Sehn LH, et al. Subgroup analysis of older patients ≥ 60 years with diffuse large B-cell lymphoma in the phase 3 POLARIX study. *Blood Adv*. 2025;9(10):2489–2499. doi:10.1182/bloodadvances.2024014707
6. Spinner MA, Advani RH. Current frontline treatment of diffuse large B-cell lymphoma. *Oncology (Williston Park)*. 2022;36(1):51–58. doi:10.46883/2022.25920940
7. Al-Sarayfi D, Brink M, Chamuleau MED, et al. R-miniCHOP versus R-CHOP in elderly patients with diffuse large B-cell lymphoma: a propensity matched population-based study. *Am J Hematol.* Published online November 28, 2023. doi:10.1002/ajh.27151